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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
FORMAN, B	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/419,817	Applicant(s) HUANG ET AL.	
	Examiner BJ Forman	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *24 August 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 23-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 23-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. This action is in response to papers filed 17 August 2000 in Paper No. 6 in which claims 1 and 10 were amended, non-elected claims 17-22 were canceled and new claims 23-38 were added. All of the amendments have been thoroughly reviewed and entered. The previous rejections under 35 U.S.C. 112, second paragraph are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102(b) are with drawn in view of the arguments. The arguments regarding the rejections under 35 U.S.C. 103 have been thoroughly reviewed and are discussed below. New grounds for rejection are discussed.

2. Currently claims 1-16 and 23-38 are under prosecution.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claim 1, 5 & 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (U.S. Patent No. 4,851,331, filed 16 May 1986).

Regarding Claim 1, Vary et al. teach a method to determine a nucleotide at a polymorphic locus in a nucleic acid sample (Column 2, lines 31-38), the method comprising amplifying a region of DNA comprising the polymorphic locus (Example 3, Column 12, lines 19-30 and primers PM and MM), wherein the primer comprises a 3' portion which is complementary to the region of DNA (Column 7, lines 23-26 and Fig. 3A) and a 5' portion which is complementary to all or part of a probe on a solid support and not complementary to the region of DNA (Column 7, lines 43-

49), labeling the amplified DNA to form labeled amplified DNA products (Column 3, lines 54-60) and hybridizing the labeled DNA products to the probe on a solid support (Column 7, lines 43-49 and Fig. 3 A and B). The claimed method steps are taught by Vary et al. wherein they differ from the only in the 5' primer sequence. Vary et al. do not teach the primer comprising a 5' portion which is identical in sequence to all of a probe on a solid support. However, detection of amplified sequences by hybridization to a solid support wherein the sequence has identity to the probes was routinely practiced in the art at the time the claimed invention was made at. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Vary et al. with routinely practice procedures and the teachings of Vary et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the 5' primer sequence of Vary et al. with a sequence identical to the probe wherein both primer sequences function in detection of amplified sequences for the obvious benefit of detecting the 5' primer sequence by probe identify for the expected benefit of sequence-specific detection. The courts have stated that in considering methods having the same method steps, it would be obvious to one of skill in the art in view of the method steps to "substitute one equivalent for another" and "express suggestion to substitute one equivalent for another need not be present to render such substitution obvious" (see *In re Fout*, 213 USPQ 532).

Regarding Claims 5 & 7, Vary et al. teach the method of Claim 1 wherein the nucleotide is radioactively labeled with ^{32}P-dATP (Column 3, lines 54-59) and epitopically labeled wherein the epitope is a halogen-modified nucleotide which is antibody-detected (Column 3, lines 63-65 and Column 4, line 66-Column 5, line2).

Response to Arguments

5. Applicant argues that Vary et al. do not teach "amplifying" which "connotes" PCR and other processes comprising two primers. This argument is not found persuasive because the claimed "amplifying" encompasses primer extension synthesis of Vary et al. In response to

applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., amplification processes comprising two primers) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant further argues that Vary et al. teach a primer having a 5' sequence complementary to the probe sequence and not identical to the probe as claimed. This argument is mooted in view of the new grounds of rejection. However, as stated above, it would have been obvious to one skilled in the art to substitute one 5' primer sequence with a sequence having the same function for the obvious benefit of detecting sequences by probe identity for the expected benefit of sequence-specific detection

6. Claims 2-4, 6, 8 & 10-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (U.S. Patent No. 4,851,331, filed 16 May 1986) as applied to claim 1 above, and further in view of Brown et al. (U.S. Patent No. 5,807,522, filed 7 June 1996), Maniatas et al. (Molecular Cloning: a laboratory manual, 1982, page 148) and Hames et al. (Nucleic Acid Hybridization: a practical approach, 1988, pages 35, 36 and 42-44).

Regarding Claims 2 & 3, Vary et al. disclose the method of Claim 1 but they do not teach the labeling couples a labeled nucleotide to the 3' end. Brown et al. teach a method to determine a polymorphism in a sample the method comprising, amplifying a DNA region comprising a polymorphic loci, labeling and hybridizing the amplified product to probes on a solid support (Column 15, lines 27-47) wherein the labeling attaches a labeled nucleotide to the 3' end (Column 15, lines 35-48 and Column 16, lines 47-54). Brown et al. teach labeling using standard means as taught by Maniatas et a. who teach labeling 3' ends of nucleotides using terminal transferase (page 148). Additionally, it was known in the art that terminal transferase specifically labels 3' end (see Hames et al. page 35-36). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Vary et al. with the teachings of Brown et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a

reasonable expectation of success to modify the incorporated labels of Vary et al. with the 3'end labeling of Brown et al. for the known benefit of terminal transferase specificity and for the obvious benefit of reducing the amount of labeled nucleotides required.

Regarding Claims 4 & 6, Vary et al. do not teach the nucleotide is labeled with fluorescence. However, Brown et al. teach the nucleotide is labeled with fluorescence (Column 15, lines 35-38) and they teach the fluorescent label is detected optically on the solid support (Column 15, lines 35-38 and Column 14, lines 11-18). Vary et al. and Brown et al. do not teach the nucleotide is labeled with an enzyme. However, enzymatically labeled nucleotides were known and routinely used in the art as taught by Hames et al. who teach the attachment of enzyme labels to nucleotides wherein the enzyme labeled nucleotides are safe, highly sensitive, inexpensive and allow rapid detection (pages 42-44). Therefore, It would have been *prima facie* obvious to one of skill in the art to modify the method of Vary et al. with the teaching of Brown et al. and Hames et al. to obtain the claimed invention because one of skill in the art would have been motivated with a reasonable expectation of success to apply the labels and detection of Brown et al. and Hames et al. for the obvious benefit of efficient, convenient and economic labeling.

Regarding Claims 10-13, Brown et al. teach the detection of Claim 8 above wherein the fluorescently labeled nucleotides at known locations on the solid support are compared and the ratio of the compared nucleotides determines the presence or absence of a mutation e.g. polymorphism (Column 15, lines 8-22) and they teach the ratio of nucleotides at two or more polymorphic loci or two or more DNA regions are determined simultaneously for two or more individuals i.e. "many patients against all known mutations in a disease gene" (Column 15, lines 19-22). It would have been ***prima facie*** obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Vary et al. with the teachings of Brown et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the method of Vary et

al. wherein a region of DNA is analyzed by the Brown et al. method wherein multiple loci, and multiple individuals are analyzed simultaneously for comparison and wherein a ratio is derived from the comparison and used to determine the presence of a polymorphic locus for the obvious benefits of eliminating the additional steps of quantitative analysis and for the expected benefit of multiple screening i.e. reduced time labor and expense as taught by Brown et al (Column 15, lines 41-43).

Regarding Claim 16, Vary et al. do not teach the method of Claim 1 wherein the solid support is a high density array. However, Brown et al. teach the solid support is a high density array i.e. microarray (Column 6, lines 32-37). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Vary et al. with the teachings of Brown et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to apply the high density array teaching of Brown et al to the method for of Vary et al. for the obvious benefit of analyzing a plurality of DNA regions simultaneously as taught by Brown et al. (Column 15, lines 19-22).

Response to Arguments

7. Applicant argues that Brown, Maniatis and Hames individually do not teach a method comprising a primer having a 5' sequence identical to all or part of a probe on a solid support. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

8. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (U.S. Patent No. 4,851,331, filed 16 May 1986) as applied to claims 1, 4, & 8 above, and further in view of Okayama et al. (J Lab. Clinical Medicine, 1989, 114(2): 105-113). Vary et al. teach the method of Claim 1 wherein multiple primers are used i.e. MM and PM (Column 12, Example 3)

and they teach each primer terminates at a distinct 3' nucleotide (Column 10, Table A, see MM-23 and PM-23)and each 5' portion is identical to all or part of a distinct probe on a solid support (Column 71, lines 26-30 and Fig. 3). Vary et al. do not teach the method comprising two primer pairs. However, Okayama et al. teach a similar method to determine a nucleotide at a polymorphic locus wherein two primer pairs are used. Specifically, Okayama et la. teach amplification of a region of DNA using two primer pairs i.e. the first pair is the Z allele primer plus the distal extension primer and the second pair is the M allele primer plus the distal extension primer (page 108, Fig. 1) wherein the first primer of each pair terminates at a distinct 3' nucleotide i.e. codon for amino acid position 342 (pages 106-108 and Fig. 1). It would have been *prima facie* obvious to one of ordinary skill in the are at the time the claimed invention was made to modify the method of Vary et al. with the teaching of Okayama et al. to obtain the claimed invention because one of ordinary skill in the art would have been motivated with a reasonable expectation of success to apply the primer pairs of Okayama et al. wherein the polymorphic region of DNA is exponentially amplified to the method of Vary et al for the obvious benefit of rapidly and specifically detecting a polymorphism from a crude sample as taught by Okayama et al. (page 112, last paragraph).

Response to Arguments

9. Applicant argues that Brown and Okayama individually do not teach a method comprising a primer having a tag (5' sequence) identical to all or part of a probe on a solid support. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

10. Claims 14 & 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (U.S. Patent No. 4,851,331, filed 16 May 1986) as applied to claim 1 above, and further in view of Lockhart et al (U.S. Patent No. 5,556,752). Vary et al. teach the method of Claim 1

wherein the probe is on a solid support (Column 4, lines 44-52) but they do not teach the solid support is a microtiter dish or beads. However, probes immobilized on microtiter dishes and beads were known and routinely used in the art at the time the claimed invention was made as taught by Lockhart et al. who teach a nucleotide detection method wherein probes are immobilized on a solid support wherein the support is beads (Column 7, lines 27-33) and microtiter dishes i.e. a polystyrene support having depressed regions (Column 8, lines 41-44 and 50). It would have It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the solid support of Vary et al. with the teachings of Lockhart et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to apply the solid support teaching of Lockhart et al. wherein probes are immobilized on microtiter dishes and beads for the obvious benefit of immobilizing probes in regionally defined and separate areas and thereby identification of hybridized nucleotides based on the region of hybridization.

Response to Arguments

11. Applicant argues that Lockhart et al. fails to fill the deficiencies of Vary et al. i.e. they do not teach a method comprising a primer having a tag (5' sequence) identical to all or part of a probe on a solid support. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

12. Claims 23. 27 & 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (U.S. Patent No. 4,851,331, filed 16 May 1986).

Regarding Claim 23, Vary et al. teach a method to prepare sample for analysis to determine a nucleotide at a polymorphic locus in a nucleic acid sample (Column 2, lines 31-38), the method comprising amplifying a region of DNA comprising the polymorphic locus (Example 3, Column 12, lines 19-30 and primers PM and MM), wherein the primer comprises a

3' portion which is complementary to the region of DNA (Column 7, lines 23-26 and Fig. 3A) and a 5' portion which is complementary to all or part of a probe on a solid support and not complementary to the region of DNA (Column 7, lines 43-49), labeling the amplified DNA to form labeled amplified DNA products (Column 3, lines 54-60) and hybridizing the labeled DNA products to the probe on a solid support (Column 7, lines 43-49 and Fig. 3 A and B). The claimed method steps are taught by Vary et al. wherein they differ from the only in the 5' primer sequence. Vary et al. do not teach the primer comprising a 5' portion which is identical in sequence to all of a probe on a solid support. However, detection of amplified sequences by hybridization to a solid support wherein the sequence has identity to the probes was routinely practiced in the art at the time the claimed invention was made at. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Vary et al. with routinely practice procedures and the teachings of Vary et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the 5' primer sequence of Vary et al. with a sequence identical to the probe wherein both primer sequences function in detection of amplified sequences for the obvious benefit of detecting the 5' primer sequence by probe identify for the expected benefit of sequence-specific detection. The courts have stated that in considering methods having the same method steps, it would be obvious to one of skill in the art in view of the method steps to "substitute one equivalent for another" and "express suggestion to substitute one equivalent for another need not be present to render such substitution obvious" (see *In re Fout*, 213 USPQ 532).

Regarding Claims 27 & 29, Vary et al. teach the method of Claim 23 wherein the nucleotide is radioactively labeled with ^{32}P-dATP (Column 3, lines 54-59) and epitopically labeled wherein the epitope is a halogen-modified nucleotide which is antibody-detected (Column 3, lines 63-65 and Column 4, line 66-Column 5, line2).

13. Claims 24-26, 28 & 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (U.S. Patent No. 4,851,331, filed 16 May 1986) as applied to claim 1 above, and further in view of Brown et al. (U.S. Patent No. 5,807,522, filed 7 June 1996), Maniatas et al. (Molecular Cloning: a laboratory manual, 1982, page 148) and Hames et al. (Nucleic Acid Hybridization: a practical approach, 1988, pages 35, 36 and 42-44).

Regarding Claims 24 & 25, Vary et al. disclose the method of Claim 23 but they do not teach the labeling couples a labeled nucleotide to the 3' end. Brown et al. teach a method to determine a polymorphism in a sample the method comprising, amplifying a DNA region comprising a polymorphic loci, labeling and hybridizing the amplified product to probes on a solid support (Column 15, lines 27-47) wherein the labeling attaches a labeled nucleotide to the 3' end (Column 15, lines 35-48 and Column 16, lines 47-54). Brown et al. teach labeling using standard means as taught by Maniatas et a. who teach labeling 3' ends of nucleotides using terminal transferase (page 148). Additionally, it was known in the art that terminal transferase specifically labels 3' end (see Hames et al. page 35-36). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Vary et al. with the teachings of Brown et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the incorporated labels of Vary et al. with the 3'end labeling of Brown et al. for the known benefit of terminal transferase specificity and for the obvious benefit of reducing the amount of labeled nucleotides required.

Regarding Claims 26, 28 & 30, Vary et al. do not teach the nucleotide is labeled with fluorescence. However, Brown et al. teach the nucleotide is labeled with fluorescence (Column 15, lines 35-38) and they teach the fluorescent label is detected optically on the solid support (Column 15, lines 35-38 and Column 14, lines 11-18). Vary et al. and Brown et al. do not teach the nucleotide is labeled with an enzyme. However, enzymatically labeled nucleotides

were known and routinely used in the art as taught by Hames et al. who teach the attachment of enzyme labels to nucleotides wherein the enzyme labeled nucleotides are safe, highly sensitive, inexpensive and allow rapid detection (pages 42-44). Therefore, It would have been *prima facie* obvious to one of skill in the art to modify the method of Vary et al. with the teaching of Brown et al. and Hames et al. to obtain the claimed invention because one of skill in the art would have been motivated with a reasonable expectation of success to apply the labels and detection of Brown et al. and Hames et al. for the obvious benefit of efficient, convenient and economic labeling.

14. Claims 31-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (U.S. Patent No. 4,851,331, filed 16 May 1986) as applied to claims 23, 26 & 30 above, and further in view of Okayama et al. (J Lab. Clinical Medicine, 1989, 114(2): 105-113).

Regarding Claim 31, Vary et al. teach the method of Claim 23 wherein multiple primers are used i.e. MM and PM (Column 12, Example 3) and they teach each primer terminates at a distinct 3' nucleotide (Column 10, Table A, see MM-23 and PM-23) and each 5' portion is identical to all or part of a distinct probe on a solid support (Column 71, lines 26-30 and Fig. 3). Vary et al. do not teach the method comprising two primer pairs. However, Okayama et al. teach a similar method to determine a nucleotide at a polymorphic locus wherein two primer pairs are used. Specifically, Okayama et al. teach amplification of a region of DNA using two primer pairs i.e. the first pair is the Z allele primer plus the distal extension primer and the second pair is the M allele primer plus the distal extension primer (page 108, Fig. 1) wherein the first primer of each pair terminates at a distinct 3' nucleotide i.e. codon for amino acid position 342 (pages 106-108 and Fig. 1). It would have been *prima facie* obvious to one of ordinary skill in the are at the time the claimed invention was made to modify the method of Vary et al. with the teaching of Okayama et al. to obtain the claimed invention because one of ordinary skill in the art would have been motivated with a reasonable expectation of success to

apply the primer pairs of Okayama et al. wherein the polymorphic region of DNA is exponentially amplified to the method of Vary et al for the obvious benefit of rapidly and specifically detecting a polymorphism from a crude sample as taught by Okayama et al. (page 112, last paragraph).

Regarding Claim 32, Okayama et al. teach the similar method wherein quantities of fluorescence at known locations on the solid support are compared wherein the known locations represent different allelic forms of the polymorphic locus having different nucleotides at the locus thereby determining a ratio of nucleotides at the polymorphic locus in the sample i.e. determining genotype (page 109). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Vary et al. with the teachings of Okayama et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the detection of Vary et al. with the detection of Okayama et al. comprising allele-specific detection and comparison for the obvious benefit of diagnosing genotype to thereby determine phenotype.

Regarding Claim 33, Okayama et al. teach the similar method wherein tow or more polymorphic loci are determined simultaneously i.e. Z allele and M allele (page 108).

Regarding Claim 34, Okayama et al. teach the method wherein the sample comprises DNA from two or more individuals (page 109).

Regarding Claim 35, Okayama et al. teach the method wherein two or more regions of DNA, each comprising a polymorphic locus are amplified (page 108-109) but they do not teach they are amplified in a single reaction mixture. However, multiple amplification reactions in a single mixture was known and routinely practiced in the art at the time the claimed invention was made. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Okayama et al. with routinely practiced procedures to obtain the claimed invention because the skilled practitioner in the art

would have been motivated with a reasonable expectation of success to modify the single amplification reaction of Okayama et al. with multiple amplifications for the known and obvious benefit of economy of labor, time and costs.

15. Claims 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vary et al. (U.S. Patent No. 4,851,331, filed 16 May 1986) as applied to claim 23 above, and further in view of Lockhart et al (U.S. Patent No. 5,556,752). Vary et al. teach the method of Claim 23 wherein the probe is on a solid support (Column 4, lines 44-52) but they do not teach the solid support is a microtiter dish, beads or high density array. However, probes immobilized on microtiter dishes, beads and arrays were known and routinely used in the art at the time the claimed invention was made as taught by Lockhart et al. who teach a nucleotide detection method wherein probes are immobilized on a solid support wherein the support is beads (Column 7, lines 27-33) microtiter dishes i.e. a polystyrene support having depressed regions (Column 8, lines 41-44 and 50) and high density array (Column 2, lines 31-34). It would have It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the solid support of Vary et al. with the teachings of Lockhart et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to apply the solid support teaching of Lockhart et al. wherein probes are immobilized on microtiter dishes and beads for the obvious benefit of immobilizing probes in regionally defined and separate areas and thereby identification of hybridized nucleotides based on the region of hybridization.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8742 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
August 31, 2000

S. Gary Jones
SUPERVISORY PATENT EXAMINER